REMARKS

Claims 12-20 have been canceled without prejudice to continued prosecution. New claims 21-30 have been added. Accordingly, upon entry of the present amendment, claims 21-30 will be pending.

The title and abstract have been amended to reflect the newly pending claims. In addition, various typographical errors have been corrected throughout the specification. The specification has been further amended to include the appropriate SEQ ID Nos and a paper copy of the sequence listing filed herewith.

Support for new claims 21-30 can be found throughout the specification and claims as originally filed. For example, support for claim 21 can be found at least at page 16, lines 11-20 and at pages 19-21. Support for claim 22 and 23 can be found at least at page 20, lines 12-28. Support for claims 24-29 can be found at least at pages 6-9, pages 17-19, and at page 21, lines 27-29. Support for claim 30 can be found at least at page 24, lines 6-21. Accordingly, no new matter has been added.

The claim cancellations requested herein should in no way be construed as acquiescence to any of the rejections and have been made solely to expedite prosecution of the application. Applicants reserve the right to pursue the claims as originally filed and/or prior to amendment herein in this or a separate application(s).

Applicants gratefully thank the Examiner for the courtesy of the interview held on June 25, 2003, with Applicants' attorney, during which the outstanding rejections of record were discussed. In particular, as noted on the Interview Summary, Applicants emphasized the lack of teaching in the prior art with respect to the use of agonistic anti-CD40 antibodies to induce antigen presenting cells (APCs)-mediated cytotoxic T lymphocyte (CTL) responses.

More specifically, the prior art fails to teach or suggest a non-blocking agonistic anti-CD40 antibody capable of inducing a CTL response. In fact, one of the few non-blocking anti-CD40 antibodies known in the prior art, mAb 5D12, had been shown to be antagonistic (*i.e.*, it inhibited CTL responses), not agonistic as presently claimed (*e.g.*, see Pasch et al., WO 02/11763, submitted herewith as Appendix A). Conversely, a number

of agonistic anti-CD40 antibodies known in the prior art had been shown to be blocking antibodies, such as mAb 5C11 taught by Zhou et al. (cited in the present Office Action), and MAb89 taught by Bjorck et al. (*Immunology* 83:430-437, submitted herewith as Appendix B). Thus, based on anti-CD40 mAbs known in the art at the time of the invention, one of ordinary skill in the art trying to generate an agonistic anti-CD40 antibody would have been motivated to have generated a blocking anti-CD40 antibody (not a non-blocking antibody, as presently claimed), since it was thought that the antibody must mimic the signal provided by the natural ligand, CD40L, which stimulates CTL responses.

Accordingly, Applicants' discovery that non-blocking anti-CD40 antibodies are capable of agonizing CTL responses was entirely unexpected. In addition, the use of non-blocking anti-CD40 antibodies provides a significant advantage in that it does not prevent natural CD40L-mediated immune responses from occurring. Thus, the claimed method of inducing a CTL response can be used as an additive therapy in the presence of CD40L, but also can stimulate CTL responses (i.e., be used therapeutically) in the absence of CD40L.

The following summary is provided to help highlight the novel and inventive aspects of the currently claimed invention:

Prior to Applicants' invention, it was understood in the art that the effector functions of CD8+ cytotoxic T cells (CTLs) are so destructive that naïve CD8+ cells require more co-stimulatory activity to induce differentiation into CTLs than do naïve CD4+ T cells which differentiate into T helper cells. Thus, differentiation of CD8+ cells into cytotoxic T cells was thought to occur in two ways. Certain virally infected dendritic cells express high levels of costimulatory molecules and induce CD8+ T cells to produce IL-2 which, in turn, drives the proliferation and eventual differentiation of these T cells into cytotoxic T cells. Alternatively, CD8+ activation by some viruses and other antigens, are thought to require the presence of CD4+ T helper cells. In these responses, both naïve CD8+ and CD4+ cells must recognize related antigens on the surface of the same antigen presenting cell. Recruitment and differentiation of the CD4+ T cell into a T helper cell results in activation of the antigen presenting cell to express higher levels of

costimulatory activity, thus enabling costimulation and differentiation of the CD8+ T cell. These two pathways are further illustrated in Appendix C.

In contrast, the present invention is based on finding that an antigen specific cytotoxic T cell response can be induced when naïve CD8+ T cells are contacted with antigen presenting cells that have been induced to mature by binding of agonist anti-CD40 antibodies. Moreover, as discovered by Applicants, agonist antibodies that do not block the binding of CD40L to CD40 are particularly effective in eliciting a cytotoxic T lymphocyte response. This finding was particularly unexpected in view of the prior art, which focused on the identification and use of anti-CD40 antibodies that mimic (i.e., compete with) CD40L for binding to CD40.

Accordingly, the currently presented claims are directed to methods of inducing a human cytotoxic T lymphocyte response by administering agonist anti-CD40 antibodies that do not block binding of CD40L to CD40. This surprising effect is clearly demonstrated by Applicants in the Examples provided in the present specification which describe working studies and corresponding data showing that maturation of antigen presenting cells can be induced using an agonist anti-CD40 antibody, *e.g.*, that does not interfere with CD40/CD40L interaction, and that these mature antigen presenting cells can induce activation of cytotoxic T lymphocytes in the absence of other components of the immune system, *e.g.*, helper T cells.

Objections to the Specification

The specification has been objected for failing to comply with the requirements for patent applications containing nucleotide sequence and/or amino acid sequence disclosures as set forth in 37 CFR 1.821-1.825. Accordingly, Applicants have submitted herewith a paper and computer readable form of the sequence listing (1 page), containing sequences which were in the specification as originally filed, to be included in the specification part of the disclosure. In addition, the specification has been amended to include the appropriate sequence identifier numbers. No new matter has been added to the application.

The specification has also been objected to based on various typographical errors. Accordingly, the specification has been carefully reviewed by Applicants and amended to correct all typographical errors, and to remove inadvertent references to Tables 1 and 2. In addition, the Title of the Invention and Abstract of the Disclosure have been amended to reflect the invention as presently claimed. Accordingly, in view of the foregoing amendments to the specification, Applicants respectfully request withdrawal of these objections.

The abstract of the disclosure has been objected to based on the ground that it does adequately describe the claimed invention. Accordingly, an amended abstract has been provided on a separate page.

Formal Drawings

The drawings have been objected to for failing to comply with the 37 CFR 1.84. Applicants respectfully submit that corrected drawings will be submitted upon the receipt of a Notice of Allowability.

Priority Date of the Claimed Invention

The Examiner maintains that the previously pending claims were not entitled to the benefit of priority to USSN 60/178,934 based on the Examiner's assertion that the priority application does not provide written support for the term "non-professional human APCs," the phrase "induce phenotypical and functional maturation of monocytes derived dendritic cells," and for the limitations set forth in claims 6 and 7.

Applicants respectfully disagree. However, to expedite prosecution, the previously pending claims have been replaced with new claims 21-30. New claims 21-30 do not contain any of the language objected to. Therefore, the objection is now moot.

Notwithstanding, Applicants maintain that the limitations objected to by the Examiner are fully supported in the priority document as filed. Specifically, support for anti-CD40 molecules (e.g., antibodies) that "enhance the stimulatory effect of CD40L on CD40 positive cells" or "can simultaneously bind to CD40 with CD40L..." or "completely inhibit CD40L binding" can be found in original claims 3-5 of USSN

60/178,934. Moreover, the summary of the invention refers to "antigen presenting cells", along with a description of both the phenotypic and functional characteristics of mature dendritic cells (i.e., professional APCs), for example, at pages 10 and 13.

Accordingly, at least for the foregoing reasons, Applicants respectfully submit that the previously claimed invention was entitled to the priority date of February 1, 2000, the filing date of USSN 60/178,934. It is also noted that this objection has not been made with respect to the presently pending claims.

Rejections under 35 U.S.C. §112, first paragraph

Claims 1-9 and 13 have been rejected on the ground that the disclosure does not reasonably convey to one of ordinary skill in the art that the inventor(s) had possession of the claimed invention at the time the application was filed. Specifically, the Examiner asserts that there is insufficient written description for "agonist anti-CD40 molecules" because the relevant identifying characteristics, such as structure or other physical and/or chemical characteristics of molecules, other than other than agonist anti-CD40 antibodies, are not set forth in the specification (Paper 7, page 4). Claims 1-9 and 13 also have been rejected on the ground that "the specification, while being enabling for 'agonist anti-CD40 antibodies' and 'CD40 binding fragments thereof,' as disclosed in the specification as filed, does not reasonably provide enablement for any 'agonist anti-CD40 molecule'." (Paper No. 7, page 7).

Applicants respectfully traverse these rejections. However, solely in the interest of expediting prosecution, claims 1-9 and 13 have been cancelled, thus rendering these rejections moot.

Applicants respectfully note that the presently claimed methods are drawn to the use of agonist anti-CD40 antibodies and/or binding fragments thereof (which the Examiner acknowledges are enabled), not to any anti-CD40 binding molecule.

Applicants further note that the presently claimed agonist anti-CD40 antibodies are defined by particular structural and functional characteristics that are fully supported by the present disclosure, as well as the disclosure of the priority application. Specifically, the present claims are drawn to methods of using anti-CD40 antibodies that

(1) bind to CD40 on antigen presenting cells (APC), (2) do not block binding of CD40L to CD40, and (3) induce APC-mediated CTL responses upon binding to CD40. As would be more than apparent to one of ordinary skill based Applicants disclosure and the working Examples described therein (and in the priority application), Applicants clearly had possession of the claimed invention at the time of filing. Moreover, based on the level of skill in the art at the time of the present invention with respect to antibody binding assays and functional T cell studies, as well as the guidance provided in Applicants' disclosure, one of ordinary skill in the art could have made and selected antibodies that bind to CD40 on APCs and induce CTL responses as claimed without undue experimentation (see e.g., pages 9-10, and pages 16-17). Accordingly, Applicants respectfully submit that the previous rejections under 112, first paragraph, are moot.

Rejections under 35 U.S.C. §112, second paragraph

Claims 1-16 have been rejected as being indefinite based on the term "APC," which the Examiner asserts should be spelled out, based on the term "non-professional APCs," which the Examiner asserts is ambiguous, and for lacking proper antecedent basis for various terms or phrases.

Applicants respectfully disagree. However, to expedite prosecution, claims 1-16 have been cancelled. Moreover, new claims 21-30 spell out the term "APC", do not contain the term "non-professional APCs," and contain proper antecedent basis. Accordingly, these rejections are now moot.

Claims 12, 13 and 16 have been rejected as being indefinite based on the use of the trade name "Deimmunized™". Specifically, the Examiner asserts that "[t]he claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product." (Paper No. 7, page 10).

Claims 12, 13 and 16 have been cancelled. Therefore, the rejection is moot as applied to these claims.

Applicants respectfully traverse this rejection as it may apply to new claim 24, which also contains the term "Deimmunized™". As stated in the M.P.E.P. 608.01(v):

> Names used in trade are permissible in patent applications if:
> (A) Their meanings are established by an accompanying definition which is sufficiently precise and definite to be made part of the claim, or
> (B) In this country, their meanings are well-known and satisfactorily defined in the literature.

In the instant specification, the term "DEIMMUNIZED™" is accompanied by a precise definition. In particular, this term is defined as referring to "antibodies in which the potential T cell epitopes have been eliminated." (page 8, lines 10-14). In addition, the specification cites International Patent Application PCT/GB98/01473 (WO 98/52976, published Nov. 26, 1998) which describes in detail the technology for making DEIMMUNIZED™ antibodies. Accordingly, the meaning of DEIMMUNIZED™ was well-known and well-defined in the literature at the time of filing.

For at least the foregoing reasons, Applicants respectfully submit that the use of the trade name DEIMMUNIZED™ is permissible in the presently pending claims and therefore request reconsideration and withdrawal of this rejection.

Rejections under 35 U.S.C. §102

(I) Claims 1-6, 9 and 15 have been rejected as being anticipated by Caux *et al.* (Research Immunology 145:235-239, 1994). Specifically, the Examiner asserts that "Caux *et al.* teach functional CD40 on B lymphocytes and dendritic cells, and that anti-CD40 antibodies can activate human progenitor and mature lymphocytes and dendritic cells." The Examiner further states that "[t]he prior art agonist anti-CD40 antibodies would have had the inherent property of binding to and stimulating professional and non-professional antigen presenting cells, including dendritic cells as well as induce maturation of dendritic cells." (Paper No. 7, page 11)

Applicants respectfully traverse this rejection. However, to expedite prosecution, claims 1-6, 9 and 15 have been cancelled. Therefore, the rejection is moot as applied to these claims.

New claims 21-30 are drawn to methods of inducing cytotoxic T cell (CTL) responses using anti-CD40 antibodies (or antigen binding fragments thereof) that do not block binding of CD40L to CD40 antigen presenting cells (APCs), such that the antibody induces an APC-mediated antigen specific CTL response in the presence of cytotoxic lymphocytes. The use of such agonistic, non-blocking anti-CD40 antibodies is neither taught nor suggested by Caux et al.

In the studies described by Caux *et al.*, B cell precursors were cultured *in vitro* with soluble anti-CD40 antibodies, in combination with either anti-IgM antibodies or phorbol esters, to examine the effect of these molecules on B cell proliferation (see p.236). In contrast, the present claims are directed to methods for inducing cytotoxic T cell (CTL) responses. Caux *et al.* do not teach or suggest a method of inducing an APC-mediated CTL cell response, let alone using a non-blocking anti-CD40 antibody, as claimed by Applicants.

Accordingly, the present claims are not anticipated by the teachings of Caux *et al.*, and reconsideration and withdrawal of this rejection is respectfully requested.

(II) Claims 1-6, 9 and 12-16 have been rejected as being anticipated by Armitage *et al.* (U.S. Patent No. 5,674,492) on the ground that Armitage *et al.* teach agonistic anti-CD40 antibodies, anti-CD40 antibodies that inhibit binding of CD40 to CD40L, and the use of combinations of antibodies. (Paper No. 7, pages 11-12)

Applicants respectfully traverse this rejection. However, to expedite prosecution, claims 1-6, 9 and 12-16 have been cancelled. Therefore, the rejection is moot as applied to these claims.

New claims 21-30 are drawn to methods of inducing cytotoxic T cell (CTL) responses using anti-CD40 antibodies (or antigen binding fragments thereof) that do not block binding of CD40L to CD40 antigen presenting cells (APCs), such that the antibody induces an APC-mediated antigen specific CTL response in the presence of cytotoxic lymphocytes. The use of such agonistic, non-blocking anti-CD40 antibodies is neither taught nor suggested by Armitage et al.

Contrary to the Examiner's assertion Armitage *et al.* teach the use of antagonistic anti-CD40 antibodies, HuCD40-M2 and HuCD40-M3, alone and in combination with soluble CD40L, to treat B cell lymphoma. Moreover, Armitage *et al.* specifically teach that these antibodies block the binding of CD40L to CD40. In contrast, the present claims are drawn to the use of agonistic anti-CD40 antibodies (i.e., antibodies that are capable of inducing APC-mediated CTL responses) that do not block the binding of CD40L to CD40.

Accordingly, the present claims are not anticipated by the teachings of Armitage *et al.*, and reconsideration and withdrawal of this rejection is respectfully requested.

(III.) Claims 1-6, 9 and 12-16 have also been rejected as being anticipated by Fanslow *et al.* (U.S. Patent 5,801,227) as evidenced by Armitage *et al.* Specifically, the Examiner asserts that Fanslow *et al.* teach that agonist anti-CD40 antibodies existed in the prior art (see column 1 Background of the Invention), and that these antibodies "would have had the inherent property of binding to and stimulating professional and non-professional antigen presenting cells, including dendritic cells as well as induce maturation of dendritic cells."

Applicants respectfully traverse this rejection. However, to expedite prosecution, claims 1-6, 9 and 12-16 have been cancelled. Therefore, the rejection is moot as applied to these claims.

New claims 21-30 are drawn to methods of inducing cytotoxic T cell (CTL) responses using anti-CD40 antibodies (or antigen binding fragments thereof) that do not block binding of CD40L to CD40 antigen presenting cells (APCs), such that the antibody induces an APC-mediated antigen specific CTL response in the presence of cytotoxic lymphocytes. The use of such agonistic, non-blocking anti-CD40 antibodies is neither taught nor suggested by Fanslow et al.

In contrast to the presently claimed invention, Fanslow et al. teach the use of anti-CD40 antibodies, CD40-M2 and CD40-M3, that block binding of CD40L to CD40 in immunoassays to detect CD40 on immune cells. Indeed these are murine forms of the same human antibodies shown to block CD40L binding to CD40 as taught by Armitage

et al.. Moreover, the authors fail to teach or suggest the use of any anti-CD40 antibody, let alone a non-blocking antibody, to induce an APC-mediated antigen specific CTL response, as claimed by Applicants. While Fanslow *et al.* refer to agonistic anti-CD40 antibodies as a means of distinguishing their discovery from the prior art, they do not teach or suggest the use of such antibodies to induce CTL responses.

Accordingly, the teachings of Fanslow *et al.* do not anticipate the presently claimed invention, and reconsideration and withdrawal of this rejection is respectfully requested.

(IV) Claims 1-4, 6 and 9 have been further rejected as being anticipated by Zhou *et al.* (Hybridoma 18:471-478, 1999) on the ground that this reference teaches agonist anti-human CD40 monoclonal antibodies that induce dendritic cell formation and maturation.

Applicants respectfully traverse this rejection. However, to expedite prosecution, claims 1-4, 6 and 9 have been cancelled. Therefore, the rejection is moot as applied to these claims.

New claims 21-30 are drawn to methods of inducing cytotoxic T cell (CTL) responses using anti-CD40 antibodies (or antigen binding fragments thereof) that do not block binding of CD40L to CD40 antigen presenting cells (APCs), such that the antibody induces an APC-mediated antigen specific CTL response in the presence of cytotoxic lymphocytes. The use of such agonistic, non-blocking anti-CD40 antibodies is neither taught nor suggested by Zhou et al.

In contrast to the presently claimed invention, Zhou *et al.* teach that particular anti-CD40 antibodies, such as 5C11, that block CD40L binding to CD40, can promote the proliferation and differentiation of adherent blood monocytes into functional dendritic cells *in vitro*. Indeed, the 5C11 antibody used in their assays was shown to have the same binding characteristics as the commercially available monoclonal antibody MAb89 (see p. 471, column 2, and p. 471, column 1, paragraph entitled "Charactization of MAb") that had been previously shown to completely block binding of CD40L to CD40 (see Bjorck *et al.*, Appendix B).

Zhou *et al.* do not teach or suggest the use of a non-blocking anti-CD40 antibody, let alone the use of a non-blocking antibody to induce an APC-mediated CTL response, as claimed by Applicants. Indeed, the studies performed by Zhou et al. were not even performed in the presence of cytotoxic T cells. Moreover, since Zhou et al. taught the use of blocking anti-CD40 antibodies (e.g., 5C11) as CD40 agonists, the authors in fact teach away from the presently claimed invention which is drawn to the use of non-blocking anti-CD40 antibodies as CD40 agonists.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

(V) Claims 1-9 and 12 have been rejected as being anticipated by Katira *et al.* (Leukocyte Typing V, Schlossman *et al.* (Ed.), Oxford University Press, Oxford 1995, page 554) on the ground that antibodies taught by Katira *et al.* would inherently have the functional limitations of the agonist anti-CD40 antibodies used in the instant invention.

Applicants respectfully traverse this rejection. However, to expedite prosecution, claims 1-9 and 12 have been cancelled. Therefore, the rejection is moot as applied to these claims.

New claims 21-30 are drawn to methods of inducing cytotoxic T cell (CTL) responses using anti-CD40 antibodies (or antigen binding fragments thereof) that do not block binding of CD40L to CD40 antigen presenting cells (APCs), such that the antibody induces an APC-mediated antigen specific CTL response in the presence of cytotoxic lymphocytes. The use of such agonistic, non-blocking anti-CD40 antibodies is neither taught nor suggested by Katira et al.

As with the cited references discussed above, Katira *et al.* fail to teach or suggest the use of a non-blocking anti-CD40 antibody to induce an APC-mediated CTL response, as claimed by Applicants. Indeed, the authors merely performed B cell proliferation studies using various anti-CD40 antibodies that bind to co-operative epitopes.

Accordingly, Katira et al. fail to anticipate the presently claimed invention and withdrawal of this rejection is respectfully requested.

Claim Rejections under 35 U.S.C. §103

(I) Claims 1-9 and 12-16 have been rejected as being unpatentable over Fanslow *et al.* and/or Armitage *et al.* and/or Zhou *et al.* and/or Caux *et al.* and/or Katira *et al.* in view of "the well known use of chimeric, humanized, DeImmunized, human antibodies at the time the invention was made, as acknowledged on page[s] 6-9 of the instant specification." Specifically, the Examiner asserts that "Fanslow *et al.,* Armitage *et al.*, Zhou *et al.* and Caux *et al.* differ from the claimed invention by not disclosing the well known use of DeImmunized and human antibodies at the time the invention was made" and "by not exemplifying combination anti-CD40 antibodies."

Applicants respectfully traverse this rejection. As discussed above, none of the cited references of Fanslow *et al.*, Armitage *et al.*, Zhou *et al.*, Caux *et al.*, or Katira *et al.* teach or suggest that a non-blocking anti-CD40 antibody can be used as an agonist, i.e., to induce an APC-mediated CTL responses. Therefore, even if these references were combined in the manner suggested by the Examiner, they would not even support a *prima facia* case of obviousness.

Indeed, the presently claimed invention was entirely unobvious in view of the teachings of the prior art. Specifically, the few non-blocking anti-CD40 antibodies taught in the prior art has either not been tested for their ability to induce CTL responses (as they would not have thought to have been agonistic since they did not mimic CD40L binding and stimulation which was believed to be required for agonistic effects), or they had been shown to be antagonists to CD40/CD40L mediated immune responses. For example, non-blocking mAb 5D12, described by DeBoer et al., had been shown to be antagonistic (i.e., it inhibited CTL responses), not agonistic. Therefore, it would not have been remotely obvious that a non-blocking anti-CD40 antibody could act as a CD40 agonist, as presently claimed.

Similarly, most of the known agonistic anti-CD40 antibodies that had been characterized in the prior art had been shown to be blocking antibodies (not non-blocking antibodies, as presently claimed), such as mAb 5C11 taught by Zhou et al., MAb89 taught by Bjorck et al. (submitted herewith as Appendix B). Thus, in view of the teachings of these references, one of ordinary skill in the art at the time of the invention

trying to generate an agonistic anti-CD40 antibody would have been motivated to generate a blocking anti-CD40 antibody, since it was thought that the agonistic effect was provided by simulating the stimulatory signal provided by CD40L.

Accordingly, Applicants' discovery that non-blocking anti-CD40 antibodies are capable of agonizing CTL responses was entirely unexpected over the teachings of the cited references, as well as other anti-CD40 antibodies known in the prior art. In addition, the use of non-blocking anti-CD40 antibodies provides a significant advantage in that it does not prevent natural CD40L-mediated immune responses from occurring. Thus, the claimed method of inducing a CTL response can be used as an additive therapy in the presence of CD40L, but also can stimulate CTL responses (i.e., be used therapeutically) in the absence of CD40L.

As previously discussed, prior to the present invention, those skilled in the art recognized two ways in which cytotoxic T cells could be activated: by dendritic cells presenting antigen in the presence of helper T cells, or by virally infected dendritic cells expressing large amounts of antigen bound to MHC class I on their cell surface. In contrast, the present invention is based on the surprising finding that agonist anti-CD40 antibodies that do not block binding of CD40L to CD40 are particularly effective at inducing CTL responses, even in the absence of either T helper cells or virally infected dendritic cells.

For at least the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of this rejection.

(II) Claims 7-16 have been rejected as being unpatentable over Fanslow *et al.* and/or Armitage *et al.* and/or Zhou *et al.* and/or Caux *et al.* and/or Katira *et al.* in view of "the well known use of chimeric, humanized, DeImmunized, human antibodies at the time the invention was made, as acknowledged on page[s] 6-9 of the instant specification, and further in view of Ledbetter *et al.* (U.S. Patent No. 6,132,992), Chang *et al.* (U.S. Patent No. 6,106,835) and Heath *et al.*(Eur. J. Immunol. 24:1828-1834, 1994).

Applicants respectfully traverse this rejection. As discussed above, the combination of Fanslow *et al.*, Armitage *et al.*, Zhou *et al.*, Caux *et al.* and/or Katira *et*

al. fail to teach, suggest, or in any way render the presently claimed invention obvious. Ledbetter *et al.* (U.S. Patent No. 6,132,992), Chang *et al.* (U.S. Patent No. 6,106,835) and Heath *et al.*(Eur. J. Immunol. 24:1828-1834, 1994) fail to make up for the above-discussed deficiencies.

Ledbetter *et al.* generally discusses bispecific antibodies that bind to a long list of possible antigens, including CD40. Chang *et al.* teach bispecific antibodies that are specific for T or B cell surface antigens CD3, TCR, CD4 and CD8, but make no mention of CD40. Heath *et al.* and Katira *et al.* teach anti-CD40 antibodies that bind to distinct epitopes. None of these references, alone or in combination, teach or suggest the use of an agonistic, non-blocking, anti-CD40 antibody, or bispecific antibody containing such an antibody, capable of inducing an APC-mediated CTL response, as presently claimed. Moreover, the use of such bispecific antibodies would have been entirely unobvious for all of the reasons described above.

Accordingly, at least for the foregoing reasons, reconsideration and withdrawal of this rejection is respectfully requested.

SUMMARY

In view of the remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Respectfully submitted,

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